Non-Invasive Genomic Profiling of Pigmented Lesions – an Interim Registry Analysis

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Abstract

Background:
Pigmented lesion analysis remains a challenging aspect of dermatology. The DermTech Melanoma Test ('the test') is a non-invasive gene-expression test designed to rule-out melanoma. It consists of the pigmented lesion assay, which detects RNA products of Long Intergenic Non-Coding RNA 00518 (LINC00518) and Preferentially Expressed Antigen in Melanoma (PRAME), and an add-on assay for DNA promoter mutations in telomerase reverse transcriptase (TERT). In previous studies, the test was found to have a negative predictive value ≥99%. This registry study examines the real-world correlation of genomically atypical (test-positive) lesions with histopathologic diagnoses.

Methods:
Between April 2021 and March 2022, multiple geographically diverse sites throughout the US submitted data to a registry to assess real-world use of the test. Approximately 8,000 clinically atypical lesions were tested. After receiving the test result, providers followed their clinical judgement for biopsy decision. Histopathologic diagnoses for biopsied lesions were correlated with test results.

Results:
Among the approximately 8000 tests performed,1033 (12.9%) were positive. Thirty-six did not have histopathologic diagnoses or confirmed test results available. Of the 997 complete cases, 134 (13.4%) were diagnosed as melanoma; 89 (66.4%) were in situ and 45 (33.6%) were invasive. Only 7 (5.2%) melanomas were beyond stage T1a. In addition, 73 (7.3%) positive lesions exhibited severe cytologic atypia or atypical junctional melanocytic hyperplasia histopathologically.

Conclusions:
Over 20% of lesions that tested positive were severely dysplastic, melanoma in situ, or invasive melanoma by histopathology. Nearly 87% of clinically atypical lesions tested negative. Almost all lesions diagnosed as melanoma were in situ or pT1a. This study demonstrates that the test guides appropriate biopsy decisions in real-world settings.

Introduction and Objective

The gene expression test is designed to rule out melanoma by analyzing non-invasively collected skin tissue from pigmented lesions for genomic atypia (LINC00518, PRAME, and/or TERT). The results of the test are designed to guide biopsy decisions on clinically suspicious lesions. This approach improves pigmented lesion management beyond visual inspection with a negative predictive value of ≥99% and a sensitivity of 91-97%, and by enriching melanoma among biopsied lesions almost 5-fold.[1-3] The real-world performance of the test and its impact on clinical practice has been addressed in a previously completed 2020 patient registry, and summarized in 2 peer reviewed publications.[3,4]

The objective of this study was to better understand the real-world utility of the test using a nationwide registry. An interim analysis of this registry is presented here.

Methods

Between April 2021 and March 2022, approximately 8000 lesions were entered into a nationwide registry from 63 unique sites. Sites were encouraged to enter all results, including corresponding histopathology.

Histopathologic diagnoses were categorized first into melanoma and non-melanoma. The melanomas were subcategorized into in situ and invasive, with the latter characterized by AJCC tumor size staging. Among non-melanomas, the number of SDN/AJMH was determined. All uncertain cases were reviewed by a board-certified dermatopathologist.

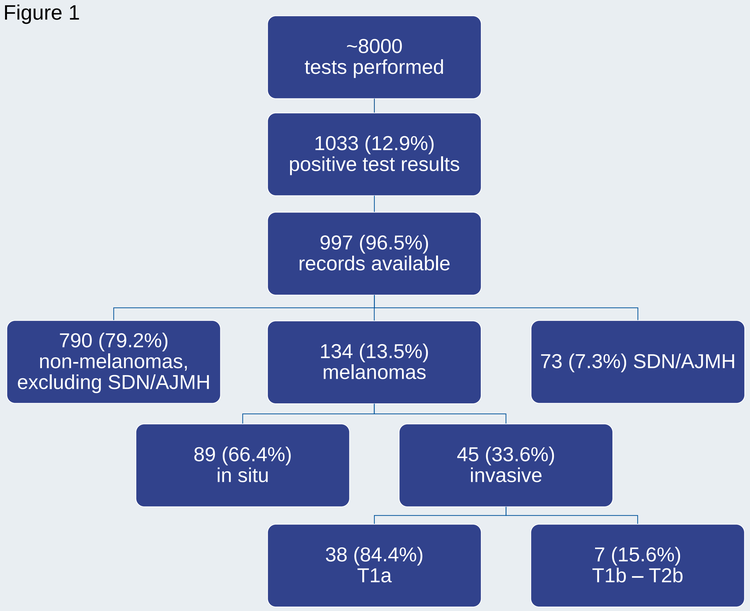
Furthermore, correlation between number of genomic markers present to histopathologic diagnoses was calculated.

Results

Of the approximately 8000 lesions entered into the registry from April 2021 to March 2022, 1033 (12.9%) were positive for at least one genomic biomarker. Thirty-six of these lesions did not have histopathologic diagnoses or confirmed test results available. Of the 997 complete cases, 134 (13.4%) were diagnosed as melanoma; 89 (66.4%) were in situ and 45 (33.6%) were invasive. Only 7 (5.2%) melanomas were beyond stage T1a. In addition, 73 (7.3%) positive lesions exhibited severe cytologic atypia or atypical junctional melanocytic hyperplasia histopathologically. These results are depicted in the Figure.

As the number of genomic markers present increased, so did the percentage of both SDN/AJMH and melanomas. Of note, the triple-positive cases (n=40) had a high likelihood of being either melanoma (n=28, 70%) or SDN/AJMH (n=6, 15%). These data are included in the Table.

Figure 1



SDN = severely dysplastic nevus
AJMH = atypical junctional melanocytic hyperplasia

Table 1.

	Genomic markers present					
	1		2		3	
	n	%	n	%	n	%
Non-melanoma (excl. SDN/AJMH)	627	87.8%	157	64.6%	6	15.0%
SDN/AJMH	45	6.3%	22	9.1%	6	15.0%
Melanoma	42	5.9%	64	26.3%	28	70.0%
Total	714		243		40	

Conclusion

This interim registry analysis demonstrates the real-world rate of positivity along with histopathologic correlation for this genomic test. Over 20% of lesions that tested positive for any number of genomic markers were diagnosed histopathologically as melanoma or SDN/AJMH. The correlation increases markedly as more genomic markers are present (12.2% for one, 35.4% for two, and 85% for three). As SDN/AJMH are often treated similarly to early melanomas, this is data that can help clinicians with their management plans.

When paired with the previously shown negative predictive value of >99%,[1,2,5] this study demonstrates the test's clinical utility. The evidence suggests that the ideal use for this test is on clinically indeterminate lesions, where the tests addition adds the greatest value with minimal risk.

Scan QR code for additional peer-reviewed publications regarding this genomic test

References

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